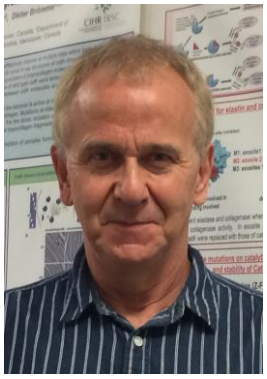

How do make safe and effective anti-resorptive cathepsin K inhibitors?

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Biosketch

Dr. Brömme received his PhD from Martin Luther University Halle-Wittenberg/GDR in 1983 and developed a life-long interest in protease research. Before joining the University of British Columbia as a Professor and Canada Research Chair in 2004, he had academic and industrial careers at the NRC Biotechnology Research Institute in Montreal, Khepri Pharmaceuticals in South San Francisco, and the Mount Sinai School of Medicine in New York. He has supervised over 80 trainees and published nearly 200 papers including book chapters and several patents with an overall H-index of 60.

Talk Synopsis

Cysteine cathepsins are powerful extracellular matrix-degrading proteases involved in musculoskeletal pathologies. Among these enzymes, cathepsin K is the best-studied drug target for osteoporosis and active site-directed inhibitors proved highly efficacious in clinical trials. However, none of these inhibitors were FDA approved due to various side effects. Our work suggests that this is due to on-target drug effects on a multifunctional protease, which can be overcome by substrate-specific, so-called *ectosteric inhibitors*. The talk will illustrate how ectosteric sites and their inhibitors were identified, how their *in vitro* and *in vivo* efficacy and specificity was characterized, and how the side effects of the cathepsin K inhibitors were overcome.